

September/October 2002

Editor:  
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# The Apothecary Bulletin

PHARMACY SERVICE & THERAPEUTICS COMMITTEES  
US ARMY MEDDAC, FORT CARSON, COLORADO

## FORMULARY CHANGES

The Pikes Peak Region Formulary Committee and the Evans Pharmacy & Therapeutics (P&T) Committee **added** the following medications to the Formulary at their September meetings:

- + azithromycin powder for injection (*Zithromax*)
- + desogestrel/ethinyl estradiol 28 tablet pack (*Mircette*)
- + donepezil 5mg, 10mg tablets, and starter pack (5mg x 42, 10mg x7) (*Aricept*)
- + etonogestrel/ethinyl estradiol (*NuvaRing*) — **restricted to OB, TMC's & AFA Cadet Clinic; OB to prepare guideline for use**
- + insulin glargine 100units/ml (*Lantus*) — **added to Basic Core Formulary**
- + losartan 25mg, 50mg, and 100mg tablets (*Cozaar*)
- + losartan & hydrochlorothiazide 50mg/12.5mg and 100mg/25mg tablets (*Hyzaar*)
- + meloxicam 7.5mg and 15mg tablets (*Mobic*) — **added to Basic Core Formulary; same restrictions for use as COX-2 Inhibitors**
- + norethindrone/ethinyl estradiol 28 tablet pack (*Eurostep Fe*)
- + pantoprazole sodium powder for injection (*Protonix I.V.*)
- + valdecoxib 10mg and 20mg tablets (*Bextra*) — **use per COX-2 Inhibitors guideline**

No medications were **deleted** from the Formulary.

As part of the ongoing drug class review process, the Pikes Peak Region Formulary Committee (with representatives from the Air Force Academy, Peterson AFB, and Evans) will conduct reviews as follows:

**November 2002** = gastrointestinal/renal/genitourinary agents

**January 2003** = central nervous system agents

**March 2003** = dermatologic/ophthalmologic agents

Pharmaceuticals submitted for Formulary consideration will be reviewed based on the above schedule. If a medication is a new entity, it may be considered earlier if submitted via a New Drug Request. Providers desiring to have input into the drug class reviews are encouraged to contact one of the Pikes Peak Committee members: **LTC Edward Torkilson (Pharmacy), MAJ Robert Gray (Family Practice), and Dr. Garold Paul (Internal Medicine).**

The next Formulary Committee Meetings will be held on Thursday, 7 November (Pikes Peak), and Tuesday, 12 November (Evans' P&T). New Drug Requests must be received by the Chief, Pharmacy Service, no later than **21 October** to be considered at the next meetings.

## HEALTH, 2002

From *Health, United States, 2002*, an annual report issued by the CDC:

- the average American infant born in 1999 is expected to live 76.7 years
- white Americans have an average life expectancy of 77.3 years, whereas African Americans average life expectancy is 71.4 years
- average life expectancy for white females is down slightly from 79.5 years in 1998 to 79.4 years in 1999
- black males born in 1999 have an average life expectancy of 67.8 years
- heart disease remains America's number-one killer, claiming 725,000 lives in 1999 (down slightly from 20 years ago)
- deaths from cancer increased by 32% between 1980 and 1999 (nearly 550,000)
- infant mortality rates remained at 7.2 deaths per 1,000 live births in 1998 (last year data available) — US ranks 28th in the world in infant mortality, down from 12th in 1960

### Q & A

What did a recent report from the *National Household Survey on Drug Abuse* show regarding the use of drugs among Americans?

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- Product Label Change
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- Recent FDA Approvals
- ADR Report
- Herb (Horse Chestnut)
- MUR Report

## COST OF NEW FORMULARY MEDICATIONS — MTF pricing

- Bextra** (valdecoxib): selective COX-2 inhibitor - indicated for OA/RA - \$1.23 per tablet (10mg and 20mg qd)
- Mobic** (meloxicam): NSAID-slightly selective for COX-2 - indicated for OA - \$0.78 for 7.5mg qd, \$0.87 for 15mg qd
- comparison: *Celebrex* 100mg \$0.62/cap; *Celebrex* 200mg \$1.23/cap; *Vioxx* \$1.23/tab (all strengths)  
 ibuprofen \$0.02/400mg, \$0.03/800mg; diclofenac \$0.08/75mg; naproxen \$0.04/375mg, \$0.05/500mg;  
 piroxicam \$0.03/20mg; sulindac \$0.17/200mg
- Cozaar** (losartan): angiotensin II receptor blocker - total dose range 25mg to 100mg (once daily or twice daily)  
 \$0.52 per tablet (all strengths)
- Hyzaar** (losartan and HCTZ): 50mg losartan/12.5mg HCTZ & 100mg losartan/25mg HCTZ - \$0.52 per tablet
- comparison: *Atacand* \$0.65/4mg and 8mg, \$0.78/16mg, \$1.06/32mg
- Eurostep Fe**: triphasic oral contraceptive with iron - \$2.04 per month
- Mircette**: biphasic oral contraceptive - \$5.65 per month
- NuvaRing**: vaginal ring contraceptive - \$14.90 per month
- comparison: monophasic - *Loestrin Fe* 1.5/30 \$0.01/month 'til 31Dec02 (\$0.35 post 1Jan03); *Alesse* \$5.96/month;  
*Demulen* 1/35 \$3.29/month; *Norinyl* 1/35 \$3.88/month; *Norinyl* 1/50 \$4.09/month;  
*LoOvral* \$7.94/month; *Desogen* \$12.65/month  
 triphasic - *Tri Leven* \$1.35/month; *Ortho Tri-Cyclen* \$6.95/month; *Ortho-Novum* 7/7/7 \$7.75/month
- Lantus** (insulin glargine): recombinant human insulin analog, extended duration of action (approx 24 hrs) - \$25.07 per bottle
- comparison: *Humalog* \$16.95/bottle; REG \$4.43/bottle; NPH \$4.43/bottle; Lente \$1.00/bottle 'til 31Dec02 (\$4.43 post 1Jan03); Ultralente \$10.89/bottle

## PRODUCT LABEL CHANGE

Wyeth Pharmaceuticals has changed the package inserts for *Prempro*, *Premphase*, and *Premarin*. The update includes recent safety information, primarily from the Women's Health Initiative, and also states that:

- ✧ these products are not indicated and should not be used to prevent coronary heart disease
- ✧ use should be limited to the shortest duration consistent with treatment goals and risks for the individual woman and should be periodically reevaluated
- ✧ when used solely for the prevention of postmenopausal osteoporosis, alternative treatment should be carefully considered
- ✧ for women who have not had a hysterectomy, *Prempro* and *Premphase* are indicated for treatment of moderate to severe vasomotor symptoms associated with menopause, treatment of vulvar and vaginal atrophy, prevention of postmenopausal osteoporosis

*"I am enough of an artist to draw freely  
upon my imagination.*

*Imagination is more important  
than knowledge.*

*Knowledge is limited.*

*Imagination encircles the world."*

~ Albert Einstein

## Q & A

Statistics from the *National Household Survey on Drug Abuse*, performed annually by the US Substance Abuse and Mental Health Services Administration, showed that the number of Americans who use drugs and alcohol rose sharply last year and teen marijuana use has reached its highest level in more than 20 years. This year's survey was tabulated using interviews with 70,000 Americans over the age of 12 years in all 50 states. Results from the survey include:

- 7.1% of the US population (nearly 16 million Americans over the age of 12 years) used illegal drugs like cocaine, marijuana, *Ecstasy*, and painkillers in 2001 (up from 6.3% in 2000)
- nearly 11% of American youths used drugs last year compared to 7.7% in 2000
- the sharpest rises occurred in the number of Americans using the mood enhancing drug *Ecstasy* (up 25% between 2000 and 2001) and the prescription pain medication *Oxycontin* (illegal use up nearly 140%)
- survey results also showed that few persons with drug abuse problems ever seek treatment = an estimated 5 million Americans needed drug treatment but did not get it and less than 10% of users believe they need help with their drug use
- adolescent marijuana use was up again last year, with more than 1.6 million 12 to 17 year olds currently using the drug



## IN THE LITERATURE...



*Archives of Physical Medicine and Rehabilitation*, September issue ... Researchers at Johns Hopkins physical medicine and rehabilitation department report that African Americans with vascular disease are up to four times more likely to have lower limb amputations than those of other groups with the same medical conditions. The investigators analyzed information on 27,149 Maryland hospital patients from 1986 to 1997 who required lower limb amputations due to vascular disease, excluding those who had a lower limb amputation due to trauma, including fractures, crash and burn injuries, bone or soft tissue malignancy, or congenital anomalies. For all levels of amputation, annual rates of amputation among African Americans were two to four times higher than whites of similar age and gender.

*Diabetes Care*, September issue ... Investigators at the University of California, San Francisco, report that partners of patients with type 2 diabetes experience at least as much depression and anxiety as the diabetic patients, especially if they are female. They studied the partners of 75 Latino and 113 European-American patients with type 2 diabetes and reported that levels of depressive affect and anxiety and rates of likely depression were as high for partners as they were for patients. They found no differences in depressive affect or anxiety by ethnicity, but they noted female partners scored higher than male partners on both measures.

*New England Journal of Medicine*, September issue ... Researchers from Harvard Medical School and Brigham and Women's Hospital along with others across the US prospectively examined total physical-activity score, walking, vigorous exercise, and hours spent sitting as predictors of incidence of coronary events and total CV events in 73,743 postmenopausal women aged 50 to 79 years (at baseline, free of CV disease and cancer). All participants completed detailed questionnaires. The researchers documented 345 newly diagnosed cases of CHD and 1,551 total CV events. Walking was linked with risk reductions similar to those associated with vigorous exercise (findings applied equally to both white and black women). Among postmenopausal women, brisk walking for at least 2.5 hours per week was linked to a 30% reduction in the risk of coronary events. The authors concluded that vigorous exercise for those wanting a higher-intensity activity should not be discouraged, but prospective data indicate walking is also linked with substantial reductions in the incidence of cardiovascular risk.

*"Always laugh when you can. It is cheap medicine."*

~ Lord Byron

### RECENT FDA APPROVALS

*Prevacid* (lansoprazole) ... for the short-term treatment of symptomatic GERD and erosive esophagitis in children 1 to 11 years of age

*Diovan* (valsartan) ... for the treatment of heart failure in patients who are intolerant of angiotensin converting enzyme inhibitors

*Ortho Tri-Cyclen LO* (25mcg ethinyl estradiol and norgestimate at 180mcg days 1-7, 215mcg days 8-14, 250mcg days 15-21) for the prevention of pregnancy; expected availability in the fall

*Lexapro* (escitalopram), the single-isomer of citalopram ... for maintenance treatment of patients with major depressive disorder

*Arimidex* (anastrozole) ... for the adjuvant treatment of early breast cancer in postmenopausal women with hormone receptor-positive disease

*Valtrex* (valacyclovir) ... for the treatment of cold sores in healthy adults

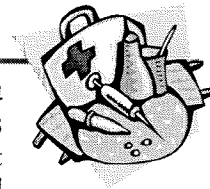
*Avapro* (irbesartan) ... for the treatment of diabetic nephropathy in people who have hypertension and type 2 diabetes

*Zelnorm* (tegaserod), a selective serotonin type-4 receptor partial agonist ... for the short-term treatment of IBS in women whose primary bowel symptom is constipation

*Eloxati* (oxaliplatin) ... for the use in combination with infusional 5-FU and leucovorin to treat metastatic carcinoma of the colon or rectum that has recurred or progressed during therapy or within 6 months of completing first-line therapy with the combination of bolus 5-FU/leucovorin and irinotecan.

*Aranesp* (darbepoetin alpha) ... for the treatment of anemia resulting from chemotherapy for nonmyeloid malignancies

## ADVERSE DRUG REACTION REPORT



There were 54 adverse drug reactions (ADRs) documented for July (n=30) and August (n=24), of which 24 (44%) were reported **spontaneously** [9 from pharmacy (outpatient and clinical); 5 from Family Practice; 3 from ICU; 2 each from Internal Medicine, PACC, and 5E; and 1 from Mental Health]. The most prevalent adverse events reported involved the anti-infective agents (n=14; 31%), the analgesic agents (n=10; 14%), and the cardiovascular agents (n=9; 14%). The anti-infective agents continue to be the top medication class involved in reported adverse events with dermatologic manifestations of the adverse events the top system involved.

One event was deemed preventable — a 38yo active duty male with a history of ibuprofen allergy took one 800mg *Motrin* for a headache (no ibuprofen prescription in CHCS for this patient) resulting in an ER visit due to hives, diffuse urticaria over face and neck, itchy eyes, and throat constriction. The patient was treated and instructed to avoid all ibuprofen products.

Four events (7%) were deemed *moderate* on the severity scale (mild, moderate, severe, fatal):

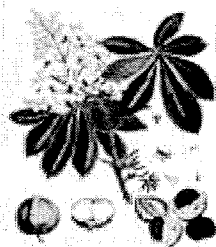
- (1) 31yo male given epinephrine for dental procedure with episode of unresponsiveness and chest pain suspected secondary to possible anxiety with hypertension +/- epinephrine administration; patient admitted for observation
- (2) 53yo male admitted due to severe oral/lingual edema with some soft palate and uvula edema due to lisinopril
- (3) 40yo male with marked bradycardia with occasional bigemy, asymptomatic, secondary to anesthesia block; patient admitted for observation
- (4) 19yo female on *Paxil* with severe depression, both suicidal and nonsuicidal thoughts, possibly exacerbated by increased *Paxil* dose; patient admitted to Pikes Peak Mental Health

Seven events were from inpatient areas:

- (1), (2), (3) above
- (4) 54yo male with SOB, wheezing post 3<sup>rd</sup> dose *Carimune* (IVIG); changed to alternative brand with pretreatment with Benadryl; reaction resolved; reaction reported to manufacturer
- (5) 29yo female complained of feeling funny, chest pressure, shaky, restless, jittery secondary to IV phenergan
- (6) 30yo male on *Crofab* (antivenom) developed hives/welts (call to Poison Center – common adverse effect); patient treated with IV *Benadryl* round-the-clock with *Crofab* continued
- (7) 54yo male with nervousness and tremor secondary to *Ultram*

***Thanks to all who continue to report adverse drug events.***

## HERB OF THE (every other) MONTH



Horse Chestnut, *Aesculus hippocastanum*, exists in nature as both a tree and a shrub, found in all temperate regions of Europe, Asia, and North America. The name *hippocastanum* is a translation referring to its ability to "cure horses brokenwinded and other cattle of coughs." Another possibility may be that it is named for the small horseshoe-like markings that are present on the branches of the tree. Both the bark and the brown nut, from which a fluid extract is made, have been claimed to be effective to strengthen and tone the circulatory system (especially the venous system), to treat varicose veins, phlebitis, and hemorrhoids. It has also been used externally as a lotion for leg ulcers. Chinese herbalists use horse chestnut not only for circulatory problems, but also as an astringent, a diuretic, to reduce edema and inflammation, and as an expectorant. The bark of young branches should be used because older bark is poisonous.

The principal ingredient in horse chestnut seed extract is a complex triterpene glycoside mixture known as "aescin" composed of acylated glycosides of protoaescigenin along with other constituents. Horse chestnut extract has been studied for its use in venous insufficiency. Diehm *et al* in 1992 gave 20 patients either placebo or 150mg aescin daily for 6 weeks and found that leg volume was significantly reduced in the treatment group and reappeared when the drug was withdrawn. Improvement in the patient's subjective symptoms (including heaviness, tenseness, leg fatigue, paresthesia) improved. Diehm *et al* in 1996 also studied 50mg aescin twice daily in a 12-week, partially blinded, placebo-controlled, parallel study in 240 patients — aescin was shown to be equivalent to compression stocking therapy in reducing lower leg edema.

The German Commission E approves the use of horse chestnut seed for treatment of complaints found in pathological conditions of the veins of the legs (chronic venous insufficiency), pains and a sensation of heaviness in the legs, nocturnal systemma (cramps in the calves), pruritus, and swelling of the legs.

The dose is 100mg to 150mg po daily of the aescin compound given in either one or two divided doses. Side effects include muscle spasms, nausea, nephropathy, pruritus and hypersensitivity reactions, urticaria, and vomiting. Severe bleeding and bruising (due to antithrombotic action of aesculin), shock, and hepatotoxicity have been reported. Use with caution with anticoagulants and aspirin due to increased risk of bleeding. Horse chestnut is contraindicated in pregnancy and breastfeeding.

**Resources:** *Complementary & Alternative Medicines* (1999), *The Review of Natural Products* (1995), Various Websites

## MUR COMMITTEE REPORT, RHONDA EUSTICE, PHARM.D

### Medication Use Evaluation — ASTHMA

#### Rationale for Study

To evaluate if the MEDCOM asthma guidelines are being followed by Evans outpatient clinics (Pediatrics, Family Practice, Internal Medicine, and Disease Management):

- long-term controllers for all patients with mild-persistent asthma (or more severe)
- documentation of asthma severity
- annual PFTs (for patients who are able to use peak flow meters)
- written action plan

#### Severity Classified

FPC	59 (80%)
IMC	25 (100%)
PED	20 (80%)
DMC	39 (100%)

#### Pulmonary Function Tests

	Performed	Too Young	Total
FPC	22/73 (30%)	14/73 (19%)	49%
PED	1/23 (4%)	12/23 (52%)	56%
IMC	10/25 (40%)	0 (0%)	40%
DMC	30/39 (77%)	7 (18%)	95%

#### Long-Term Controllers

All services 100%

#### Written Action Plans

FPC	10/73 (14%)
PED	2/23 (9%)
IMC	2/25 (8%)
DMC	32/39 (82%)

#### Conclusions:

- 100% of patients seen for asthma were given inhaled steroids.
- In the March 2002 review, the number of patients who had annual PFTs was less than 20% of patients seen in Pediatrics, FPC, and IMC. This review showed an increase in PFTs by over 20% for all services.
- Asthma severity was documented in the medical record in over 80% of the medical records of asthma patients seen in Pediatrics, FPC, and IMC — an increase since the March 2002 review. Note: for the first review, only specific provider notes were reviewed; in the second review, if severity was mentioned in the master problem list or on any chart note, this was included.
- Written action plans were given to 82% of patients seen in the DMC, 8% seen in the IMC, 14% seen in the FPC, and 9% seen in Pediatrics. Note: written action plans are given based on personal best peak flows and many patients were too young to use peak flow meters.

#### A little bit of history ...

- 1817 ... James Parkinson first described Parkinson's Disease as "paralysis agitans"
- 1822 ... Robert Koch identified the tubercule bacillus by techniques of culturing and staining
- 1847 ... chloroform was introduced by James Simpson, a Scottish obstetrician
- 1867 ... Lauder Brunton first described the use of inhaled amyl nitrite to stop an acute attack of angina
- 1884 ... the tetanus bacillus was discovered by Nicolaier
- 1885 ... a vaccine against rabies was developed by Pasteur
- 1902 ... the laxative effect of phenolphthalein was discovered by Vamossy when he was studying it as a possible additive to artificial wines - it was introduced as a laxative preparation in 1953

## MUR COMMITTEE REPORT, RHONDA EUSTICE, PHARM.D (CONTINUED)

### Proton Pump Inhibitor Use – PROVIDER PROFILES

#### Purpose:

*Prilosec* (omeprazole) was taken off the EACH formulary and replaced by *Aciphex* (rabeprazole) in August 2001. In December 2001, a patient telephone survey was conducted to evaluate the effectiveness of *Aciphex* for GERD. At that time, it was thought that *Aciphex* may not be equivalent to *Prilosec* on a milligram-per-milligram basis. Since that review, new guidelines have been distributed to the EACH providers. This review was conducted to evaluate EACH providers adherence to these guidelines.

EACH guidelines for the use of Proton Pump Inhibitors state:

- 1) trial of *Aciphex* 20mg daily; if not effective, increase to *Aciphex* 40mg
- 2) if not effective, change to *Prevacid* 30mg daily for 30 days
- 3) if not effective, change to *Prilosec* 20mg daily (nonformulary)

#### Conclusions:

- Only 14% of patients receiving *Prilosec* had been given a trial of *Aciphex* and/or *Prevacid* per CHCS & chart review.
- Only 50% of patients receiving *Prevacid* had been given a trial of *Aciphex* per CHCS & chart review.
- 22 of 26 providers prescribing *Prevacid* were > 90% compliant with the guidelines; 10 of 16 providers prescribing *Prilosec* were > 90% compliant with the guidelines.

### PYXIS Review – UPDATE

#### June 2001 review:

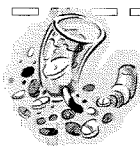
A medical record review of patients receiving medications via the PYXIS machine in the Emergency Room was performed in June 2001 to assess the use of the PYXIS machine. It was discovered that medications being dispensed from the ER were not being documented correctly. It was found later that this was not only a problem in the ER, but in all areas where PYXIS machines were utilized. ***This was a significant violation of JCAHO standards and prevented pharmacist review of after-hours dispensing.***

#### Changes made:

- Controlled medications:
  - 1) A pharmacy technician audited various inpatient records from ER, 5E, ICU, and Anesthesia. It was found that there were many discrepancies in all areas.
  - 2) The ER started reviewing their own records. Since they have been doing this, they have caught and corrected their own discrepancies.
- Other Medications:
  - 1) Non-controlled medications held in the ER have been moved to the FLEX machine which requires the providers to enter an order into CHCS. The label is then scanned into the FLEX machine which dispenses the medication.

#### Conclusion:

- Peer review of PYXIS usage has proven to work well.
- It is easier to track the medication usage in the ER since the FLEX machine is now being utilized.



### *Drug Interaction Corner*

#### **Selected Fluoroquinolone Drug Interactions**

- ⇒ decreased GI absorption of quinolone: sucralfate, iron salts, didanosine, antacids
- ⇒ decreased elimination of quinolone: cimetidine, probenecid, azlocillin
- ⇒ other:
  - ◆ quinolones & NSAIDs = increased risk of CNS stimulation and convulsive seizures reported with enoxacin and NSAIDs
  - ◆ quinolones & anticoagulants = decreased clearance of R-warfarin
  - ◆ quinolones & theophylline = decreased theophylline clearance and increased plasma levels and symptoms of toxicity seen with theophylline and ciprofloxacin
- ⇒ mechanism unknown:
  - ◆ sparfloxacin/gatifloxacin/moxifloxacin & antiarrhythmic agents = risk of life-threatening cardiac arrhythmias including torsades
  - ◆ sparfloxacin & drugs that prolong QTc interval = risk of life-threatening cardiac arrhythmias including torsades
  - ◆ ofloxacin & procainamide = increased procainamide plasma concentration
  - ◆ ciprofloxacin/norfloxacin & cyclosporine = increased cyclosporine toxicity